STATE MEDICAID P&T COMMITTEE MEETING

FRIDAY, August 17, 2007
7:00 a.m. to 8:30 a.m.
Cannon Health Building
Room 132

MINUTES

Committee Members Present:

Lowry Bushnell, M.D.	**Kort DeLost, R.Ph.**
Karen Gunning, Pharm. D.	**David Harris, M.D.**
Raymond Ward, M.D.	**Duane Parke, R.Ph.**
Jerome Wohleb, Pharm. D.	

Board Members Excused:

Thomas Miller, M.D.	**Koby Taylor, Pharm. D.**

Dept. of Health/Div. of Health Care Financing Staff Present:

RaeDell Ashley	**Duane Parke**
Jennifer Zeleny	**Lisa Hulbert**
Doug Springmeyer	

Other Individuals Present:

Lyle Odendahl	Chris Beckwith, U of U	Linda Tyler, U of U
Drew Heincy, Merck & Co.	Jim Hoover, Bayer	Tom Holt, Schering-Plough
Eric Nalder, Santaurus	Trish McDaid-O'Neill, AstraZeneca	Mark Pasos, Santaurus
Gerry Shioshida, Schering-Plough	Robb Host, Cephalon	Tim Hambacher, Abbott
Dr. Jim Griffin, Santaurus	Roy Lindfield, Schering Plough	Rob Wood, Pfizer
Erika Brumleve, GSK	Matthew Hansen, M.D.	Barbara Boner, Novartis
Corbett Carver, Pfizer	Craig Boody, Lilly	Kurt Maymard, TAP
Matt Johnson, Takeda	Bart Watts, TAP	Kathryn Ryan, AstraZeneca
Cap Ferry, LEC	Mandy Hosford, AstraZeneca	Lori Howarth, Bayer
Tung Vu, Student	Tony Molchan, Abbott	Erin Mitchell, Student
Roy Palmer, Pfizer	Martin Tenlen, AZ	Shelby Fletcher, Pfizer
Robin Campbell, Merck Schering-Plough	Linda Craig, Astra Zeneca	Alan Baily, Pfizer

Meeting conducted by:

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1. Introduction of New Member: Dr. David Harris is a pediatrician at Granger Clinic. He has been in practice since 1984. He is a representative for the Intermountain Pediatric Society.

2. Minutes for June 2007 were reviewed, corrected, and approved.

3. DUR Board Guidelines: Duane Parke addressed the Committee. The Division provided the P&T Committee with a draft of bylaws with which to govern the Committee. Committee members were asked to consider the draft over the next month.

   The DUR Board has passed the P&T Committee Guidelines. The Committee members were provided with a copy of Rule 414-60B. They were asked to look at item #7, Clinical and Cost-related Factors. The P&T Committee shall base their decisions on the following clinical and cost-related factors established by the DUR Board: If clinical and therapeutic factors are substantially equal, then the P&T Committee shall recommend to the Division of Health Care Finance that it consider only cost; if the cost information available to the P&T Committee that the costs are substantially the same, then the P&T Committee makes a recommendation to the Division of Health Care Finance based on the clinical and therapeutic profiles of the drugs; and in making recommendations to the Division of Health Care Financing, the P&T Committee may also consider whether the clinical therapeutic effects and medical necessity requirements justify the cost differential between drugs in a therapeutic class. The DUR Board did accept this rule, and it will be used to govern the P&T Committee at this time.

4. Organizational Issues:

   a. Chairperson Election: Duane Parke addressed the Committee. Karen Gunning had been elected as a temporary chairperson, because not all of the members of the Committee had been seated at the time. Since then, all eight members had been seated. The P&T Committee must now elect a new chairperson or sustain Karen. The Committee unanimously sustained Karen Gunning as a chairperson.

   b. Meeting Times: Duane Parke addressed the Committee. For September 2007, the Division has reserved room 132. For the remainder of 2007, the Division has reserved room 114 for the third Friday of each month. For 2008, the Division has scheduled room 125. Committee members agreed that the third Friday of each month would be the best time to hold meetings.

   c. Website/Handouts: Duane Parke addressed the Committee. The website address was provided on this month's P&T Committee agenda. Duane stated that he will try and post the handouts given to P&T Committee members on the website as soon as they are emailed to Committee members, so that anyone else can see what the Committee is receiving.

5. Schedule for Committee Consideration of Drug Classes: Duane Parke addressed the Committee. The Committee was presented with a proposed schedule of drug classes to consider. This schedule was prepared by the University of Utah Drug Information Center under the advisement of the P&T Committee. The P&T Committee unanimously accepted the schedule as proposed.

6. Methodology: Duane Parke addressed the Committee. The P&T Committee will be using the evidence-based drug information that is found on the Oregon Health Sciences University website. The Division also has a contract with the University of Utah Drug Information Center to provide additional evidence-based information and back-up information for the Committee. Duane asked the Committee members to vote on using these two sources as the primary sources of drug information. Duane also stated that presentations to the Committee

should be limited to information that has been peer-reviewed and published. Written information should be forwarded to the University of Utah Drug Information Center. Public comments will be limited, due to the time constraints of an hour-and-a-half meeting. The Committee unanimously voted to use the Oregon Health Sciences University publications and the University of Utah Drug Information Center as primary sources for evidence-based drug information.

7. Public Comment:

a. Dr. Shioshita of Merck/Schering-Plough addressed the Committee. The use of Vytorin in high-risk to very high-risk patients with arteriosclerosis is complementary to a generic strategy. Guidelines for high-risk and very high-risk patients have been changed. The LDL goals for these patients should be <100 with the option of <70, based on new data. Dr. Shioshita provided handouts with data showing most commonly prescribed strengths of common Statins. Generic statins are good for low- to medium-risk patients who need LD reductions < 50%. The higher doses of the branded statins Crestor and Lipitor provide a greater reduction. The starting dose of Vytorin 10/20 gives an LDL reduction > 50%. In head-to-head trials comparing simvastatin and Vytorin, Vytorin provided greater reductions in LDL. Even at 80mg, simvastatin did not provide a 50% reduction. Vytorin is superior to simvastatin in getting high-risk to very high-risk patients to goal.

b. Dr. Feras Bader of the University of Utah addressed the Committee. There are two schools of thought regarding statins in cardiology. One school of thought believes that the effects of statins are purely related to LDL reduction. The other school of thought believes that the medications have their own pleiotropic effects in addition to LDL reduction. Cardiovascular medicine is learning every day that different medications in this class has different effects than other medications in that same class. There is also evidence for phased medicine. While there are different statins available for reducing LDL, there are also different medications reducing LDLs. Dr. Bader believes in emphasizing outcomes as a basis for using a one medication versus another medication. Lowering LDL by itself is an important aspect of statin therapy, not all medications have the same outcome. Dr. Bader's sub-specialty is heart failure and heart transplant. There is only one statin, atorvastatin, that is FDA-approved for reduction in heart failure admissions. This is based on the recent TNT trial. Dr. Bader's goal is to encourage the P&T Committee to continue with the strategy of utilizing evidence based medicine and looking at outcomes as the primary decision-making point when discussing statin access for patients. Dr. Bader sees many Medicaid patients, and would like to see that patients have access to statins based on outcomes rather than just LDL reductions. Cost is one issue, but he really believes that outcomes, LDL reductions, safety, and efficacy play very important roles.

c. Dr. Mandy Hosford from AstraZeneca Cardiovascular Medical Affairs Division addressed the Committee. AstraZeneca is committed to recognizing the right patient for Crestor. This is the patient who is not at LDL goal with current therapy; may be hypertensive, diabetic, or have a history of a prior cardiovascular event; arteriosclerosis in the carotid, coronary, or peripheral vasculature. The Crestor patient can be a high-risk or at-risk patient. About 80% of diabetics reach their goal with Crestor. Crestor is treating high LDL and low HDL. When this is done, the underlying disease of arteriosclerosis, which leads to cardiovascular events, is being

treated. There is published data for rosuvastatin that shows the real-world effectiveness of Crestor in large managed care populations. There is greater efficacy with Crestor over Lipitor or Zocor. Failure to reach LDL goal is a driver for potential non-adherence to therapy, as well as represents a therapeutic treatment gap. AstraZeneca has identified in these real-world comparative effectiveness studies patient factors that are not predictive of achieving goal, for example, the need of a > 30% LDL reduction, as well as a baseline high-risk. In these managed-care studies, Crestor continues to get more patients to goal than other available statin monotherapies. Referring to safety, this is a very safe class as a whole. Recognizing that this is a safe class, adverse events are seen with untoward drug-drug interactions. Crestor, like Pravachol, is very minimally metabolized; it does not go through the P450-3A4 metabolic machinery, so it puts Crestor in a very good setting for preventing drug-drug interactions that could lead to adverse events. Regarding outcomes, Crestor has an ongoing outcomes trial with heart failure patients that is in its very late stages. This is looking at reducing heart attacks and reducing cardiovascular death in patients on low-dose Crestor in patients with heart failure.

d. Dr. Kate Ryan from AstraZeneca addressed the Committee. While Nexium is effective, and more effective than all of the other PPI's across all grades of erosive esophagitis and at reducing the symptoms of GERD, AstraZeneca realizes that in the studies, Nexium is much more effective in the more severe classes of erosive esophagitis. AstraZeneca recognizes cost limitations with regard to the State managed care plans and other health professionals, so a generic strategy is supported. For patients with a more severe level (LA Grade C & D), that is where use of Nexium is most appropriate. Certainly, Nexium is appropriate in all grades A-D, data shows significantly greater effects in the more severe grades, so that is where Nexium's resources will be focused. AstraZeneca will support a generic strategy in the lower grades.

e. Roy Palmer, Medical Director with Pfizer addressed the Committee regarding atorvastatin. Dr. Bader emphasized the importance of outcomes. Pfizer has long-term outcomes data from 3-5 year studies from over 80,000 patients. The highest available dose of 80mg has outcomes data from over 14,000 patients. This is across every patient type that will be seen and prescribed a statin in a clinic: primary prevention, secondary prevention, acute coronary syndrome, diabetes, hypertension, etc. Pfizer has examined every patient population that they consider likely to get a statin. This is the data that has driven some of the recent guidelines. The NCEP Committee issued a white paper, and that was primarily based upon Lipitor data. Lipitor is the only statin that has done research on some of the lower LDL numbers. There are two high-risk patient populations on which the only positive data is available with Lipitor. Those are with acute coronary syndrome patients and stroke patients. The only other studies to examine those groups are with simvastatin, and those came out as neutral studies. So, for many physicians, the only evidence-based choice for acute coronary syndrome patients and stroke patients is with 80mg of atorvastatin. Not only does this provide good information about the prevention of cardiovascular events with Lipitor, it also gives a great deal of information about the safety of Lipitor. Not all drugs in the same class behave the same way. They have different pharmacokinetics, different safety profiles, and different drug interactions. The only way to really know what a drug does is in long-term studies that examines many patients over many years. Lipitor has done that. LDL and goal attainment are

surrogate endpoints. Once there is outcomes data, from an evidence-based perspective that should be the primary consideration. There are some other practical considerations. CMS data indicates that about half of the patients that are on a high-potency statin in Utah Medicaid are receiving Lipitor right now. If these patients are switched, according to the package insert, it is recommended that they have liver function tests before the switch and 12 weeks after the switch. The P&T Committee should consider if switching will cause an unnecessary number of office visits and lab tests, especially if titration is considered. Another consideration should be the patent of Lipitor. The patent expires in March 2010, and there is a reasonable chance that a generic will be available at that time. If patients are switched now, there is a chance that they will be switched back to generic atorvastatin. This will generate even more unnecessary office visits and labs in another 2&1/2 years. Continued access to Lipitor, based on available outcomes and safety data, is requested.

f. Dr. Janet Harsberger, a pediatrician, had submitted comment by email. Duane Parke read the comment to the Committee. She stated that she likes to have soluble tablets and powders available for PPI's.

g. Dr. Matt Hansen, an internist, addressed the Committee. Diabetic patients and those at highest risk need to be able to have access to the high potency statins, rosuvastatin and atorvastatin, to be able to get to goal. This is very important for evidence-based medicine, to be using medications that have data to back them up. In particular, atorvastatin, has significant data to back up the utilization in patients with diabetes. In terms of costs, generic simvastatin is appropriate in many patients and prescribed to these patients. But for high-risk patients, specifically diabetics, it is important to have something that will get the patients to goal and has data to support it.

The Committee asked Dr. Hansen what cutoff he uses before he considers a diabetic patient high-risk and need a high-potency statin. Dr. Hansen considers all of his diabetic patients to be high-risk and treats them to an LDL goal of <70. In those patients he looks at the starting LDL to determine what percentage reduction is needed. If the reduction needed is > 30%, he will initiate treatment with a high-potency statin. He does not believe that generic pravastatin or simvastatin can achieve this reduction.

The Committee pointed out that the preferred versus non-preferred designation will mean available versus not-available. Non-preferred agents will still be available to physicians who designate that the patients need that medication.

h. Dr. Hugh Griffin, from Santorus Medical Affairs, addressed the Committee about Zegerid. All proton pump inhibitors are acid labile. Proton pump inhibitors prior to Zegerid employed enteric coating, making them delayed release. Zegerid is a unique delivery system, which utilizes sodium bicarbonate rather than enteric coating, to protect the omeprazole from degradation by stomach acid. As demonstrated in clinical studies, this ensures that the immediate release micronized omeprazole has full absorption within 30 minutes. Zegerid provides the longest acid control of any proton pump inhibitor, according to the FDA approved label information, of 18.6 hours. Additionally, in head-to-head studies, results indicate that Zegerid is faster and more effective than Nexium, Prevacid, and Protonix in controlling stomach acid during the night, which is the most difficult period to control stomach acid. When

looking at Zegerid's acceptance in other managed care organizations, it is available in many Medicaid formularies, including California, Florida, and Vermont. It is also available on the formularies of United Health Care, Wellcare, Pacificare, and Sierra Health Plan. Adverse events are very similar to other proton pump inhibitors. Zegarid does contain sodium, so care must be given to patients with sodium restricted diets. Prepared summaries and a dossier with all of the necessary references were submitted to the Committee.

8. Committee Considerations of High Potency Statins: Karen Gunning addressed the Committee. Dr. Ward had previously made a motion to put drugs into one of three categories: preferred with no copay, preferred, and non-preferred. Many patients would like to have no copay, particularly in classes such as PPI's that are on the lower end of need. This would be appropriate, especially in that class, because there is one agent that is significantly cheaper than all other agents in that class. Duane Parke stated that the Division will not consider waiving the copay for any medications at this time. Karen Gunning asked if the Committee could make a motion to waive the copay at this time, even though it may not be implemented. The Committee could make such a motion.

Dr. Ward made a motion that Committee recommendations place medications in one of those three categories: preferred with no copay, preferred, and non-preferred. The motion was passed unanimously.

Karen Gunning stated that, based on information provided by Medicaid, a majority of the patients in Medicaid (46%) are on atorvastatin. Of these patients, 2/3 are on either 10mg or 20mg. While information presented to the Committee about high-risk patients is very important, there is a large majority of patients on lower doses of these high-potency statins. Based on this information, the Committee should consider how the evidence pertains to these patients. These patients may not be at goal, but this is the current state of practice in Utah. Karen asked if there were any motions on how to place these medications into Dr. Ward's scheme of classification.

Dr. Ward made a motion that the Committee consider lovastatin as preferred no copay; Vytorin, simvastatin, and other generics as preferred; Lipitor, Crestor, and other brand-name statins that have an available generic as non-preferred. It was pointed out to Dr. Ward that simvastatin is just as cheap, if not cheaper, than lovastatin. Dr. Ward amended his motion that all preferred agents have a copay.

Duane Parke pointed out that the Division can seek supplemental rebates from the manufacturers. Karen Gunning stated that the P&T Committee needs to determine if all of the agents are equally safe and efficacious. She asked Dr. Ward to explain his groupings in terms of safety and efficacy. Dr. Ward stated that the University of Utah Drug Information Center showed good equivalence on safety data in the class. The manufacturers have also provided good information to the Committee to give an idea of how much effect can be gotten from the different doses. Many patients can be well served by one of the generics. When patients need to get to a lower target, Vytorin seems to be the natural choice because it has very good lowering, and it is easier to tell patients that their statin will be staying the same and something will be added to it. Particularly with older and more frail patients, it is nerve-wracking for them to have the statin changed at the same time. In the absence of cost data, these are the most important considerations. Duane Parke stated that all of the bids put the high-potency statins in the same ballpark. That being the case, Dr. Ward stated that the

easiest drug for patients to transition to from the lower-potency drugs is Vytorin.

The Committee asked if there was good evidence-based information to support the use of Vytorin. Dr. Ward stated that he felt that he was content with the information provided at the last P&T Committee meeting.

Dr. Tyler stated that the Oregon review did not specifically cover Vytorin, but that the University of Utah could provide information on that agent.

Karen re-stated the motion that was proposed by Dr. Ward. The motion was to include all of the generic agents and Vytorin on the preferred list, and all of the other branded statins as non-preferred. Dr. Tyler pointed out that the Committee is trying to make the determination if the statins are all equal for lipid lowering. The Division would then pick on agent based on contracting issues. The statins are complex because there may be two different levels of how patients are treated. Patients who are treated initially may be treated one way, while patients who need marked lipid lowering or do not respond to initial treatment might need to be treated the second way with a high-potency strategy. If there is a group of drugs that needs to be considered in the high-potency strategy, it is the job of the Committee to determine which of the drugs should be used in a high-potency strategy, and which drugs are considered in the overall strategy. If cost were not an issue, could any of these drugs be used as the first line strategy? When talking about preferred versus non-preferred, it would be helpful to think about differences in efficacy and safety if all of the agents cost the same.

Karen Gunning stated that differences in patient acceptability in his patient population are an important consideration. She asked Committee members if there were any other differences that were felt to be important in this class of drugs. Committee members said that lipid lowering guidelines should be considered. Karen Gunning pointed out differences in how lipid lowering guidelines may be interpreted.

Dr. Ward felt strongly that generics should be favored over any branded statins, even if bids make the costs comparable, because products with generics available encourage competitive pricing in a free marketplace. Duane Parke stated that the Division is considering placing MAC pricing restrictions on some of the generics as Maine has done. For example, the MAC on generic simvastatin is around 35 cents. Kort Delost pointed out that it is cheaper for retail pharmacies to stock generics, such as simvastatin. Retail pharmacies do not buy branded statins at the same dead-net cost as Medicaid after rebates, so profitability and carrying costs are more favorable with generics. Therefore, Dr. Ward's generic strategy is favorable, if all of the agents are therapeutically equal.

Dr. Tyler asked the Committee members if there are any clinically meaningful differences in the ability of these drugs to lower lipids in equipotent doses. Dr. Ward stated that, in his opinion, at equipotent doses his answer is no. Duane Parke re-read the statement in the rule that "If clinical and therapeutic factors are substantially equal, then the P&T Committee shall recommend to the Division of Health Care Finance that it consider only cost". This is a two-stage decision process, so the Committee needs to make a recommendation based on clinical differences, and the Division will then strategize the class based on cost.

Dr. Ward re-stated his motion. In terms of efficacy, he would make a motion that all of the agents that are available as generic are equally efficacious as a first-line therapy. All of the branded agents are equally efficacious as a second-line therapy. In terms of a

recommendation of a preferred branded agent, he would recommend Vytorin, for the reasons stated earlier.

The Committee stated that the safety of Vytorin, particularly as it pertains to the ezetimibe component during pregnancy, be considered.

Dr. Ward made a first motion that drugs available as generics are all similar in their efficacy and safety. Duane Parke stated that all of the lower potency statins will be covered, and the Division does not need recommendations on these since all of the generics will be covered.

Dr. Ward made a new motion that all of the high-potency statins are similar in their potency. Dr. Ward made a second motion that Vytorin be the preferred agent in the high-potency class and that Crestor and Lipitor be non-preferred. The Committee felt that there was more research available for Lipitor than the other statins to make an evidence-based decision. Karen Gunning re-stated that the available data on Lipitor in the community suggests that Lipitor is not really being used as a high-potency statin. Dr. Ward also feels that there is a very low bar for physicians wishing to prescribe lower doses of high-potency statins to be able to write "medically necessary - dispense as written" and still be able to get the non-preferred drug. In that regard, the P&T Committee is creating guidelines rather than barriers for prescribers in the community.

Duane stated that under Dr. Ward's proposed motion, the department would actually loose money. The bids for secondary rebates are all within pennies of one another. However, if the Division designates a particular agent as non-preferred, a secondary rebate cannot be collected. The reason for having a preferred drug list is, if all the drugs are equal, to save money and collect secondary rebates. It happens that for this class, the Division can cover them all and collect secondary rebates and save money. The Committee does not have the cost information for these agents.

Karen gunning summarized that in terms of whether or not there are significant differences in safety and efficacy of these drugs, the first motion is that there are not. The second motion is, given that Medicaid can choose any one of these drugs, is there another drug or group of drugs that this Committee feels must be preferred in order to address patients that need more significant lipid lowering. For the purposes of the minutes, the drugs that are being considered in the high-potency group are simvastatin, Lipitor, Crestor, and Vytorin.

The first motion is that there are not significant differences in the safety and efficacy of the drugs. The motion passed unanimously.

The second motion is, given that Medicaid can choose any one of these drugs, is there another drug or group of drugs within the four high-potency statins that this Committee feels must be preferred in order to address patients that need more significant lipid lowering. For patients who need extreme reductions, Crestor and Vytorin may provide that. Dr. Ward made a motion that all four of the high-potency statins are equal, and one of those four must be on the list. The motion passed unanimously.

9. Proton Pump Inhibitor Presentation by the University of Utah Drug Information Center: Dr. Tyler addressed the Committee. The proton pump inhibitors are a class of drugs that decrease gastric acid and gastric secretory volume. Omeprazole was the first drug in this class, introduced in 1989. Since then, there have been four other PPI's introduced to the

market: lanzoprazole, pantoprazole, rabeprazole, and esomeprazole. In 2003, omeprazole went over-the-counter in the United States.

PPI's are used to treat a variety of gastric conditions, including peptic ulcer disease both duodenal and gastric, gastroesophageal reflux disease, healing of erosive esophagitis, and prevention of drug-induced ulcers. Likewise, if h-pylori is part of the diagnosis, then PPI's are given in combination with antibiotics to eradicate h-pylori. Predominant use for PPI's is in GERD and gastritis. For GERD, which causes the heartburn acid regurgitation, the American Gastroenterological Association recommends that patients first try lifestyle modification, antacids, and over-the-counter H2 antagonists. If that doesn't work, then PPI's or high-dose H2 antagonists can be tried.

Oregon's process is that they work with a panel to develop the key clinical questions that need to be considered in evaluating the class of drugs. They key questions are identified, and a literature search is conducted. They go through the articles and determine what is the relevant data for the questions that they are looking at. They then rate all of the data. In this particular case, they also conducted a meta-analysis of the data to answer some of the key clinical questions. The graph of the meta-analysis is in the back of the hand-out. In this particular case, there were over 3,000 citations from the literature search. They excluded 2,490 of those. Of the 580 articles that were retrieved and reviewed, 68 were head-to-head trials, 95 were trials with active controls or combination therapy, 11 were placebo controlled, and 18 were systematic reviews that were included in the literature. An additional 22 articles were included to elucidate on some of the background and methods, and some of the information on drug interactions.

The first clinical question was what is the comparative efficacy of PPI's in patients with symptoms of GERD. One of the problems with this class of drugs is that there are many endpoints that are used in the studies. The Committee members were advised to read the background information on the various endpoints that were used in the studies and some of the controversy. The first endpoint is symptom relief and esophagitis healing. In the 12 head-to-head trials, there was no difference between omeprazole, lansoprazole, rabeprazole, pantoprazole in the outcome of complete symptom relief at four weeks. The only significant difference was on esomeprazole 40mg and omeprazole 20mg, and there was a 10% difference between groups. In several of these trials, esomeprazole was better, but many believe that this is a dosing issue, as comparative doses were not used in these trials. Esomeprazole 40mg was also compared to lansoprazole 30mg and pantoprazole 40mg for complete symptom relief, and there were no significant differences when those comparisons were made.

Time relief of heartburn was similar for all PPI's. 13 different trials of PPI's versus H2 blockers and 3 systematic reviews found the four PPI's to be equally effective.

In the prevention of relapse, there are no comparative differences between omeprazole, lanzoprazole, and rabeprazole. The Langland study looked at those over four years and compared omeprazole and rabeprazole. Two 6-month studies found differences between esomeprazole 20mg and lansoprazole 15mg, this is a dosage issue, and pantoprazole 20mg. Pantoprazole was more effective than ranitidine in one 12-month trial and esomeprazole was more effective than ranitidine in a 6-month trial. This is why many people prefer PPI's to H2 blockers.

In a group, looking at the results based on baseline severity among patients with moderate to severe esophagitis at baseline, esomeprazole 40mg was more effective at healing esophagitis at 4 and 8 weeks than omeprazole 20mg (again, that dosage thing) and lanzoprazole 30mg. The pooled risk difference of 3 studies of omeprazole 20mg versus esomeprazole 40mg showed a little bit of a difference. But again, there is a dosage difference there.

The Committee members asked if there was a reason to design a study with non-equipotent doses. Dr. Tyler stated that the postulates around that is to demonstrate that one's product is superior to a competing product, especially if a company is trying to get the product on the market. Many of the cox-2 studies were designed to demonstrate that even higher doses of the cox-2's were safer than traditional NSAID's. In terms of GI toxicity that was a good strategy when the drugs were coming to market.

Key question 1B was in the comparison of differences in the PPI's to H2 blockers. PPI's were more effective in healing than H2 blockers, but there were no differences among the PPI's for any comparisons.

The second key clinical question asked is there a difference in the efficacy of peptic ulcer disease and NSAID-induced ulcers. In the summary of the evidence, there were 9 head-to-head trials that were reviewed. Omeprazole and lansoprazole had similar effectiveness for endoscopic healing and symptom relief. The evidence for rabeprazole, pantoprazole, and esomeprazole is less strong because there are only single studies that evaluated this. No study found significant differences in healing rate. Looking specifically at gastric ulcer, rabeprazole was compared to omeprazole and there were no differences in healing rate. For NSAID-induced ulcers, there were 2 studies with esomeprazole, one that compared esomeprazole and rabeprazole, and no significant differences were noted. In terms of preventing NSAID-induced ulcers, there did not appear to be differences between omeprazole, lanzoprazole, and pantoprazole. Getting into this group of key clinical questions, not all drugs were studied, but no differences were found based on the drugs that were studied.

The third key question was related to adverse effects: are there comparative incidence or nature of complications of the different PPI's for patients being treated for GERD, peptic ulcer, and NSAID-induced ulcers? The comparative evidence on long-term effects is limited. There are no long-term head-to-head trials designed specifically to look at adverse events. In the two trials that were longer-term (48 weeks and 5 years) there were no differences found between omeprazole and lanzoprazole. In a 6 month study of esomeprazole and lansoprazole, there were no significant differences in adverse events. In long-term studies of individual drugs, no important differences were apparent, but comparisons across the studies are not always clear.

Key question number four asked if there are subgroups of patients based on demographics, other medications, or comorbidities in which one medication is more effective or associated with fewer adverse effects. The head-to-head comparisons did not adequately describe or analyze any subgroups that we might care about for differences in effectiveness, but two addressed differences in adverse events based on age, gender, race and found no differences.

The overall summary, based on Oregon's review of the exhaustive literature search that they did is summarized in table 13 in the handout. In general, there is very little evidence that

there is any difference in the safety or effectiveness in the PPI's in the general population or any relevant subgroups. A majority of the studies had fair internal validity, but poor external validity with highly selective patient populations selected for those particular studies.

10. Committee discussion of Proton Pump Inhibitors: Dr. Ward stated that he felt like based on what was presented, the Committee could make a recommendation to the Division that there are no differences among the PPI's, and the Division should make a decision based on cost. Karen Gunning stated that she would like to hear some safety information about the sodium bicarbonate/omeprazole combination, because this may be an issue for patients that are sodium restricted. Dr. Tyler stated that the University of Utah will address those questions in the next P&T Committee meeting.

    Karen Gunning also stated that the Committee may want to consider the special population of children, which was not addressed by the Oregon review. Dr. Harris stated that many children cannot swallow a capsule until age 6-10, and that the Solu-tab preparations are used in children. Dr. Tyler stated that she would be happy to address that in the next P&T Committee meeting.

    Discussion and votes on Dr. Ward's motion were deferred until the next P&T Committee meeting.

Next Meeting Set for Friday, September 21, 2007.
Meeting Adjourned.

Minutes prepared by Jennifer Zeleny